

High Throughput Technologies to Break the Biological Barriers to Cellulosic Fuels

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A recent paradigm shift in biological science research is from characterizing single genes or proteins (over an investigator's career) to studying whole genomes, proteomes or pathways in single "experiments" in a few months. It has been known for some time that while it is quite straightforward to clone and characterize a single gene. However, it is a completely different matter to perform detailed functional and structural studies in parallel for a few hundred genes, metabolic pathway or whole genome. The ability to produce proteins is currently a major biological, physical, and computational challenge in protein research. Given a standard set of conditions, less than 30% of any given genome is expressible in a recombinant host. Protein expression requires complex, lengthy procedures, and specific proteins commonly require individual strategies for optimal expression. Standard bench-level procedures for protein production (expression and purification) do not exist. This lack of validated processes leads to a lengthy search for correct vector, host, expression and purification conditions to yield protein in milligram amounts. This problem is further compounded during metabolic engineering experiments where not only proteins have to be expressed, in addition genetic and regulatory processes have to be optimized for successful production of a product. To this end the technologies division has been developing comprehensive suite of technologies in a consolidated facility. These successful methods and workflows are aimed at directed cloning methods for generating large numbers of expression constructs for protein expression and purification, screening of libraries for enzyme engineering and metabolic engineering. These processes will improve technical performance, productivity and reduce costs to allow affordability and timely progress towards our goals. We discuss some of these process development efforts and present initial results.

